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Patent Application

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1. Description of Invention

Manufacturing method of various organic amine salts of 2,3-diphosphoglyceric acid

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Specifications

1. Description of Invention

Manufacturing method of various organic amine salts of 2,3-diphosphoglyceric acid

2. Scope of Patent Claim

The production of organic amine salts from 2,3-diphosphoglyceric acid by the reaction of 1-(isopropylamino)-3-(1-naphthoxy)-2-propanolol, adenosine, 2-diphenylmethoxy-N, N-dimethylethylamine, or 2.6-bis-(diethanolamino)-4,8-dipiperidinopyrimido-(5.4-d)-pyrimidine with 2,3-diphosphoglyceric acid.

3. Detailed Explanation of Invention

2,3-diphosphoglyceric acid is widely distributed in microbes, plants and mammals, specifically, high numbers are found in the red blood cells of mammalian species.

This invention produces new types of organic amine salts of 2,3-diphosphoglyceric acid by reacting 2,3-diphosphoglyceric with organic amines such as 1-(isopropylamino)-3-(1-naphthoxy)-2-propanolol, adenosine, 2-diphenylmethoxy-N, N-dimethylethylamine or 2.6-bis-(diethanolamino)-4,8-dipiperidinopyrimido-(5.4-d)-pyrimidine.

Organic amine salts of 2,3-diphosphoglyceric acid obtained by this invention are new chemical compounds. Their physiologically active effects (especially effects related to prevention of thrombus formation) are made stronger through a synergistic action than those same effects produced by 2,3-diphosphoglyceric acid. These chemical compounds are extremely useful as drugs for the medical treatment of arterial thrombosis, angina pectoris, and related arterial diseases, as well as medicaments that act in the prevention of blood clots associated with hemodialysis.

The chemical properties of the organic amine salts of 2,3-diphosphoglyceric acid produced by the invention are shown in Table 1.

Table 1.

Name of Base	Molecular Formula	Analytical Values (N%)	
		Theoretical Value	Observed Value
Adenosine	$C_{13}H_{21}N_5P_2O_{14}$	13.13	14.02
2-diphenylmethoxy-N, N-dimethylamine	$C_{34}H_{71}N_2P_2O_{13}$	4.07	3.86
2.6-bis-(diethanolamino)-4,8-dipiperidinopyrimido-(5.4-d)-pyrimidine	$C_{27}H_{48}N_6P_2O_{14}$	14.55	15.03
1-(isopropylamino)-3-(1-naphthoxy)-2-propanolol	$C_{35}H_{50}N_2P_2O_{14}$	5.33	5.84

Next, an explanation is given of the details of the invention with recourse to practical examples.

Practical Example 1

3g of adenosine is added to 4 ml of water and 3g of 2,3-diphosphoglyceric acid is added while the mixture undergoes agitation. The adenosine crystals will dissolve immediately. When ethanol is added to this aqueous solution white crystals are precipitated. 5.2g of adenosine salt of 2,3-diphosphoglyceric acid is produced with a melting point of 200°C and above (transition color change to black) when the material in the ethanol water solution is recrystallized.

Practical Example 2

10g of OH type JRA-400 is added to an ethanol solution of 3g hydrochloride of 2-diphenylmethoxy-N, N-dimethylethylamine. After one hour of agitation the solution is separated. When an ethanol solution of 1g 2,3-diphosphoglyceric acid is added to this ethanol solution, a white colored sediment is immediately produced. The heated ethanol is recrystallized, which produces 3.2g crystal salt of 2-diphenylmethoxy-N, N-dimethylethylamine from 2,3-diphosphoglyceric acid with a melting point of 250°C and above.

Practical Example 3

10g 2,6-bis-(diethanolamino)-4,8-dipiperidinopyrimido-(5,4-d)-pyrimidine is dissolved in 10ml ethanol. When an ethanol solution containing 3g 2,3-diphosphoglyceric acid is added to this solution, yellow-orange crystals are precipitated. When recrystallized from a large quantity of ethanol, 6g 2,6-bis-(diethanolamino)-4,8-dipiperidinopyrimido-(5,4-d)-pyrimidine salt of 2,3-diphosphoglyceric acid with a melting point of 250°C and above (characteristic resolution) is obtained in the form of yellow crystals.

Practical Example 4

3g hydrochloride of 1-(isopropylamino)-3-(1-naphthoxy)-2-propanolol is dissolved in 30ml alcohol. 25g of OH type JRA-400 is added and agitated for one hour. Upon filtration, 1.5g 2,3-diphosphoglyceric acid is added to the filtrate. Subsequently, ether is further added to the solution. The precipitated crystals are filtered out. The precipitant is recrystallized in an ethanol acetone liquid mixture and 3g of the amine salt of 2,3-diphosphoglyceric acid is obtained.

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5. Index of Attached Documents

(1) Application Judgement Claim Form
(2) Specifications Form
(3) Power of Attorney
1 copy each

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